Letters to the Editor
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Global medicines shortage: The European perspective

Corresponding Author:
Name: Richard Price
Email: richard.price@eahp.eu

Dear Editor,

It is with great interest that we learned of the special edition of your journal to investigate the global medicines shortage problem.

In respect of the international discussion we thought your readers may be interested in some of the work recently conducted in this area at the European level.

Responding to increasing concern from members about the problem, the European Association of Hospital Pharmacists (EAHP) conducted a survey in 2012-13 to better understand the scale and nature of the medicines shortage problem from the European hospital pharmacy perspective. With over 300 responses from 25 countries, the results were stark:

- 99% of hospital pharmacists across Europe are experiencing problems with medicines shortages;
- 63% say the problem is a weekly, sometimes daily occurrence; and
- 77% say the problem has become worse in the last year.[1]

Colleagues from the Pharmaceutical Group of the European Union (PGEU), representing community pharmacy in Europe, also surveyed their membership. They discovered that although some countries are more affected than others, medicine shortages have been reported by all respondents to the survey and the problem is increasing. According to the survey, a broad range of medicines is affected, including even basic medication such as aspirin. The survey suggested that the prevalence of medicine shortages has increased in the past year- just in the UK over one million branded medicine supply failures occur each year.[2]

Armed with this information, EAHP and PGEU then combined with a range of patient organisations, such as the European AIDS Treatment Group, and Health Action International, in an initiative led by the European Public Health Alliance (EPHA), to present the problem to Members of the European Parliament, European Commission and others at a high profile event in Brussels in May 2013.[3] Separate investigatory work is also being conducted via a patient and professional collaboration under the aegis of the European Medicines Agency.

With awareness of the problem now beginning to be raised in Europe, in the year ahead it is crucial that we move into a mode of solution-finding and implementation, if the end user of medicines, the patient, is not to suffer greater problems in terms of access and treatment. Our research has already revealed concerning stories of unnecessary treatment delays and switches endured by patients in acute conditions.

From a global perspective, some of the useful solutions we have discussed and proposed include:

- greater understanding by governments and national regulators of the critical impacts medicines shortages have in relation to patient welfare and safety;
- better information collection and dissemination about the nature of the shortages problem;
- investigation of the impact that national strategies on medicines pricing and reimbursement are having on the operation of the supply chain; and
- sharing of best practices between countries in terms of responding to the problem (e.g. early warning systems and information portals)

On this last point, we note the action taken in the USA via the supply chain provisions of the 2012 Food and Drug Administration Safety and Innovation Act (FDASIA), such as enhanced early notification and reporting requirements. We look forward to future assessment of its impact, and the anticipated publication of reports by the Food and Drug Administration and Government Accountability Office on the problem which are mandated via sections of the Act. It is clear that what we are dealing with is a global problem, and so it is imperative that the lessons in regulatory response and research from one country are shared quickly and effectively with others.

It must also be hoped that special editions of journals such as your own can play their part in disseminating relevant information and pin-pointing the remedial measures that can be most effectively taken.

Thank you for the invitation to contribute. We congratulate the editorial team on their initiative and look forward to reading and learning from the publication.

Dr Roberto Frontini
President of the European Association of Hospital Pharmacists (EAHP)

Monika Kosinska
Secretary General of the European Public Health Alliance (EPHA)

References

1. Price R. 99% of HPs experience medicines shortages in past year. Brussels, EAHP; 2013, February 21. Available from: http://www.eahp.eu/press-room/99-hps-experience-medicines-shortages-past-year.
2. Chave J. Medicine Shortages: Medicine Shortages is a Global Public Health Problem. Brussels, PGEU, 2013. Available from: http://www.pgeu.eu/en/policy/20-medicine-shortages.html,
3. Can EU citizens afford their medicines ? The economic crisis and access to medicines in Europe [www.epha.org]. c2013 [updated 2013 May; cited 2013 Aug 28]. Available from: http://eventstream.streamovations.be/can-eu-citizens-afford-their-medicines.php

Zinc Supplementation for Severe Bronchiolitis: A Randomized Controlled Trial

Corresponding Author:
Name: Piyush Gupta
Email: prof.piyush.gupta@gmail.com

Dear Editor,

Immune boosting properties of zinc are known, and its role in diarrhoea is well established. Literature is scarce regarding the role of zinc in bronchiolitis.[1,2] We conducted this double blind randomised placebo controlled trial to evaluate the efficacy of zinc in children (three months to two years) with severe bronchiolitis. Ethical clearance was obtained from the institutional ethical committee.

Bronchiolitis was defined and categorised as per the clinical definition of acute onset of rapid breathing with wheezing and/or crackles in a young infant with a prodromal upper respiratory catarrh.[3] Severe bronchiolitis was labelled in the presence of any of the following: inability to feed, severe distress, marked chest retractions, nasal flaring, grunting, apnoea, hypoxemia (oxygen saturation <92%), lethargy, altered sensorium, irritability or cyanosis in room air. Children with previous episode of wheeze or having received bronchodilator therapy; and those with underlying cardiac or chronic pulmonary disease, severe malnutrition, meningitis, or consolidation were excluded. Children having received any micronutrient supplementation within last four weeks were also excluded. Eligible children were randomised (using block randomisation) to receive either zinc (20 mg/5mL) or placebo in suspension form. Both syrups were identical in appearance, taste and odour. Oral zinc or placebo was administered as 2.5 mL/day (infants less than six months) and 5 mL/day (6-24 months) once daily for seven days.

Baseline data included detailed clinical history, vital signs (temperature, heart rate, respiratory rate, and blood pressure), assessment of breathing effort, cyanosis, mental status, chest auscultation, and anthropometry (weight, length, head circumference). Respiratory rate was counted for 60 seconds. Baseline oxygen saturation was measured using a pulse oximeter in room air. All children were hospitalised and received treatment as per standard protocol for treatment of severe bronchiolitis according to Guidelines of Indian Academy of Pediatrics that included IV fluids, oxygenation, antipyretics and nebulised epinephrine.[1] Inhaled salbutamol was administered as per the decision of treating physician. The child's condition was assessed every eight hours for presence of tachypnea, wheezing, chest indrawing, cyanosis, oxygen saturation, inability to feed, and lethargy.

Primary outcome measures included:

- time to resolution of severe bronchiolitis, defined as when lower chest retractions and the danger signs (inability to feed, lethargy, cyanosis or hypoxia) were no longer present; and
- (ii) time to resolution of individual symptoms/signs of severe bronchiolitis (lower chest indrawing, fast breathing, inability to feed).

Secondary outcome measures included durations of hospitalisation, IV therapy, and oxygenation. Kaplan Meier survival plots were constructed to compare median duration of each outcome variable by log rank test.

Means and proportions were compared by student's *t*-test and chi-square test (or Fischer's exact test), respectively.

Figure 1 depicts the study flow chart detailing the inclusion of subjects in the study. At enrolment, participants in both the groups were comparable for age, sex, anthropometric parameters, duration of symptoms, respiratory rate, and oxygen saturation (Table 1).

Table 1: Baseline Parameters in Zinc and Placebo Group

Parameters	*Total (N=100)*	*Zinc (N=26)*		*Placebo (N=74)*	*Mean difference*	*95% CI*	*P-value*
	Mean±SD	*Mean±SD*	*N*	*Mean±SD*			
Age of child (months)	5.7±3.0	6.1±4.3		5.5±2.4	0.65	(-1.16,2.47)	0.47
Weight (kg)	6.3±1.1	6.5±1.1		6.2±1.1	0.24	(-0.26, 0.75)	0.34
Length (cm)	63.9±5.1	64.2±5.9		63.8±4.8	0.42	(-1.9,2.74)	0.72
Weight for age Z-score	-1.62±1.0	-1.44±0.89		-1.68±1.04	0.23	(-0.22, 0.69)	0.31
Length for age Z-score	-1.23±1.20	-1.27±0.97		-1.21±1.3	-0.06	(-0.61, 0.5)	0.84
Weight for length Z-score	-1.09±1.29	-0.87±1.15		-1.16±1.34	0.29	(-0.3,0.87)	0.33
Duration of symptoms (days)	4.2±2.40	3.6±1.94		4.4±2.51	-0.84	(-1.92, 0.24)	0.12
Respiratory rate (breaths/min)	73.0±8	73±10		73±7.	0.41	(-3.20, 4.03)	0.82
SpO_2	91.4±3.15	91.9±3.60		91.3±2.98	0.61	(-0.81, 2.04)	0.40
pH	7.5±0.05	7.5±0.06		7.5±0.05	-0.004	(-0.04, 0.03)	0.85
PCO_2	29.5±7.68	26.3±5.33		30.2±8.02	-3.92	(-8.88, 1.04)	0.11
PO_2	76.2±27.25	9	88.0±35.78	73.2±24.33	14.76	(-5.52, 35.03)	0.15

Mean (SD) duration of supplementation in the zinc and placebo groups were 4.5 (1.61) and 4.8 (1.61) days, respectively. Median time taken for resolution of severe bronchiolitis (95 per cent CI) was 46 (33-59) hours in the zinc group as compared to 40 (36-44) hours in the placebo group (*P*=0.37). Clinical resolution in both the groups was also comparable for all the other outcome measures (Table 2). No major adverse effects were noted. Only one child had vomiting and another had diarrhoea that lasted two days; both the children belonged to the placebo group. Our study thus documented that short term supplementation with zinc in severe bronchiolitis, given during the course of illness, starting from day 1, does not help in resolution of severe bronchiolitis.

Table 2: Comparison of Primary and Secondary outcome variables in Zinc and Placebo Group

Parameters	*Zinc*			*Placebo*			P value
	Median	SE	95% CI	Median	SE	95% CI	
Time to Resolution of severe bronchiolitis (hours)	46	7	33-59	40	2	36-44	0.37
Time to Resolution of lower chest indrawing (hours)	46	7	33-59	40	2	35-45	0.35
Time to Resolution of fast breathing (hours)	64	10	44-84	72	5	62-82	0.90
Time to Resolution of inability to feed (hours)	16	2	11-21	8	0	8-8	0.19
Duration of hospitalisation (hours)	80	8	64-96	96	4	88-104	0.96
Duration of IV fluid (hours)	32	2	28-36	32	2	27-37	0.51
Duration of O_2 therapy (hours)	16	3	10-22	16	2	13-19	0.79

Brooks, et al. have shown that adjunct treatment with zinc accelerates recovery in pneumonia.[1] Subgroup analysis on wheezy children (one-third of the total) showed that zinc supplementation did not affect either duration of severe pneumonia or overall length of hospital stay for wheezy children. Our results are similar

to the only other double blind randomized study that also concluded no benefit of zinc in bronchiolitis.[2] A major limitation of our study was smaller number of patients in zinc group due to randomisation failure and there is a possibility that the significance levels may work out differently if more cases had been recruited. Since bronchiolitis is a disease of healthy children, these children are unlikely to be zinc depleted and benefit from zinc supplementation, which could be a plausible explanation for negative results. This needs to be studied further. Until then, inadvertent use of zinc in children with bronchiolitis should be restricted.

Sincerely,

Jhajharia Arvind, Batra Prerna, Shah Dheeraj, Sharma KK*, Gupta Piyush.
Department of Paediatrics and *Department of Pharmacology
University College of Medical Sciences and Guru Tegh Bahadur Hospital, Delhi -95, India

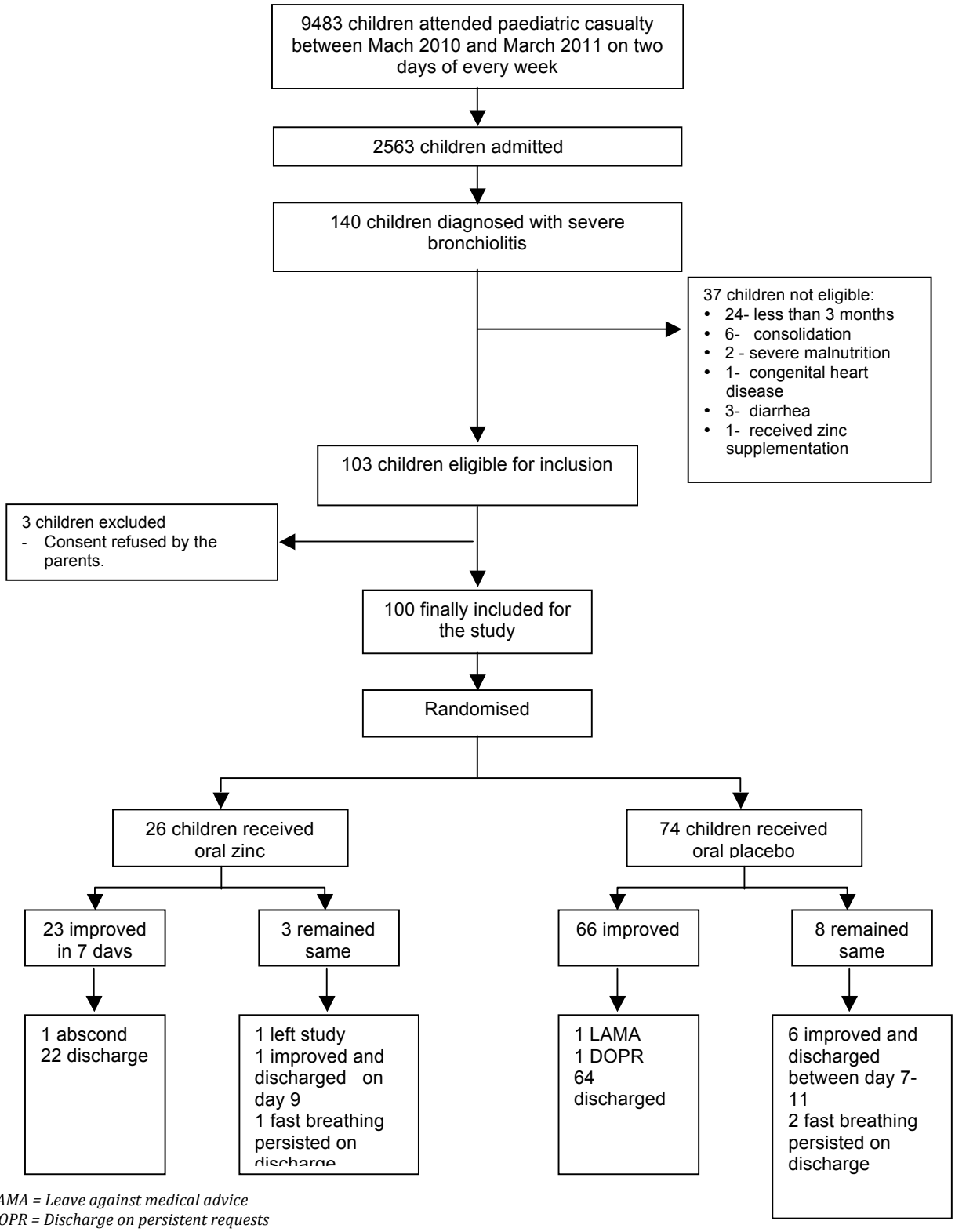
References

1. Brooks WA, Yunus M, Santosham M, Wahed MA, Nahar K, Yeasmin S, Black RE. Zinc for severe pneumonia in very young children: double-blind placebo-controlled trial. Lancet 2004;363:1683-8.

2. Heydarian F, Behmanesh F, Daluee M, Kianifar H, Hematian M. The role of zinc sulfate in acute bronchiolitis in patients aged 2 to 23 months. Iran J Pediatr. 2011 ;21:231-4.

3. Agarwal R, Singh V, Yewale V. RTI Facts. IAP Consensus Guidelines on Rational Management of Respiratory Tract Infections in Children. Mumbai: Indian Academy of Pediatrics; 2006.

Figure 1: Consort diagram



LAMA = Leave against medical advice
DOPR = Discharge on persistent requests

Workshops on helping students learn medical ethics – brief report

Corresponding Author:
Name: Rano Mal Piryani
Email: r_piryani@yahoo.com

Dear Editor,

This report outlines the content of a workshop conducted over two-half days for the faculty for preparation of implementing medical ethics course held at KIST Medical College, Lalitpur, Nepal on June 5 & 6 2013. It also gives information at a glance about implementation of the medical ethics course in South and South-East Asia as ethical aspects for taking health care decisions may be overlooked, considered irrelevant or ignored in South and South-East Asia.

Ethics is a branch of philosophy dealing with values pertaining to human conduct, considering the rights, wrongs, and motives of such actions. Medical ethics helps define the values and guidelines governing decisions in medical practice.

Medical ethics has developed over many centuries. In the allopathic practice of medicine, its development commenced from the time of Hippocrates and over time several "codes of conduct" have been developed. Health care decisions are based on clinical, technical and ethical grounds. Most of the time healthcare professional take decisions on clinical and technical grounds but ethical issues involved may either be overlooked, considered irrelevant or unnoticed.

Understanding the principles and practice of medical ethics is a very important aspect of the education of a medical professional. The advances in medical technologies and their cost and potential to cause harm have increased the importance of learning about medical ethics. The significance of understanding and applying medical ethics is very relevant to a medical professional due to a diversity of reasons, including increasing litigation, changes in complexities in medical practice and the importance of consumer courts. A change in the relationship between medical professionals and their patients, increasing public awareness due to increase in literacy ratio, access to internet, awareness campaign on various issues by consumer and civil society has further enhanced its importance.

KIST Medical College (KISTMC), a newly established medical school in the private sector affiliated with Tribhuvan University (TU) follows the curriculum of the Institute of Medicine (IOM) updated in 2008. Medical ethics is one of the new courses included in updated curriculum. The course of medical ethics needed extra preparation as it was a new addition in the curriculum and faculty from different disciplines had to be involved in its implementation. This workshop on "helping students learn medical ethics" was organised on June 5 & 6 2013.

The overall aim of the workshop was to get prepared for the implementation of the medical ethics course. The specific objectives were: 1) to familiarise the faculty to the curricular requirements in medical ethics; and 2) to orient them to the learning resources available for teaching the subject and provide them the opportunities to practice using learning resources to facilitate students' learning in medical ethics.

Twelve faculty members participated in the workshop- one each from the department of Medical Education, Forensic Medicine, Community Medicine, Clinical Pharmacology, Obstetrics and Gynaecology, Clinical Anatomy, Paediatrics, General Surgery, Clinical Psychiatry, Internal Medicine, Family Medicine and Nephrology. Four resource persons- the known medical educationists from Nepal facilitated the workshop.

Modalities used for conducting workshop were:
1. Presentations by the resource persons on role of ethics in medical education and its importance, course outline, outline for lesson plan, teaching/learning methods to be used, assessment methods to be used, how to use the module & facilitators' guide, and resources material used for teaching/learning and assessment.
2. Group discussion.
3. Group work for the preparation of microteaching on a section of the course of medical ethics by participant faculty.
4. Practice on microteaching and feedback from the group and resource persons.
5. Resource material provided for reference (20.1 COURSE TITLE MEDICAL ETHICS TU_IOM Curriculum 2008, Module for teaching Medical Ethics to undergraduate and Facilitators' guide for teaching Medical Ethics to undergraduates).

The participants presented lessons on informed consent, medical negligence, patients' rights, end-of-life decision, pharmaceutical promotion, ethical aspects of transplantation and organ donation, ethical aspects of

treating patients with HIV/AIDS, ethical issues in reproductive health, ethical issues in prenatal diagnosis and end-of-life decision in neonatal intensive care.

Faculty members were oriented about curriculum of medical ethics, teaching/learning and assessment methods to be used to facilitate students learning while conducting sessions on different aspects of medical ethics, and better and purposeful use of resource material. Curriculum of medical ethics was made structured Outline for implementation of medical ethics curriculum was prepared. Teaching methods to be used were finalized- tutorial, small group discussions (SGDs), role-playing, demonstrations, integrated ward classes/ward-based teaching, debates, any other suitable method faculty wishes to chose. Assessment methods to be used were also finalised: feedback from the students through the use of feedback forms, reflection of students through reflective log, integrated assessment during clinical case assessment, use of clinical scenario, any other suitable method faculty wishes to chose. A strategy for implementing the course was finalised; the session for students of final year MBBS will start from June 16, 2013.

It is expected that this activity will be effective in helping students acquire required knowledge and skills to practice medicine ethically.

Sincerely,

Piryani Rano Mal[1], Thapa Trilok Pati[2], Piryani Suneel[3]
KIST Medical College, Lalitpur, Kathmandu Valley, Nepal

References

1. Curriculum for Bachelor of Medicine and Bachelor of Surgery Tribhuvan University Institute of Medicine. Revised in 2008 published by Medical Education Department, Institute of Medicine, Kathmandu, Nepal.
2. Module for teaching Medical Ethics to undergraduate. Published by World Health Organization Regional Office for South-East Asia- SEA-HSD-321. 2009.
3. Facilitators' guide for teaching medical ethics to undergraduate students in the South-East Asia Region. Published by World Health Organization Regional Office for South-East Asia- SEA-HSD-330. 2010.